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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/675,828	09/29/2000	Thomas J. Cummins	CDS-266	1041

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 12/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/675,828	CUMMINS ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29,33 and 36-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,29,33 and 36-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This office action is in response to an amendment filed on August 25, 2003. Claims 28, 29, 33 and 36 were pending. Applicants amended claims 33 and 36, and added new claims 37-40. Claims 28, 29, 33 and 36-40 are pending and will be examined. Applicants amendments overcame the rejection of claims 28, 29, 33 and 36 under 35 U.S.C 112, second paragraph.

2. The terminal disclaimer filed on August 25, 2003 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of the U.S. Patent No. 6,174,668 has been reviewed and is accepted. The terminal disclaimer has been recorded. Therefore the double patenting rejection of claims 33 and 36 has been rendered moot by the terminal disclaimer.

3. Applicant's arguments with respect to claim 36 have been considered but are moot in view of the new ground(s) of rejection. This office action is made non-final because of new grounds for rejection.

Claim interpretation

4. The meaning of the terms "about 2° C" or "about 5° C" was not defined by Applicants. Therefore, for example, "about 2° C" may mean 3° C, 4° C, 5° C, etc. Further, Applicants' formula given in claims 33 and 37 has been used to calculate the melting temperatures in Frank et al. reference, since the use of the formula is required by the claim limitation.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 37-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 37-39 are indefinite in claim 37. Claim 37 is indefinite over the recitation of "from 90 to 400 nucleotides as measured or 3' to 3'..." (lines 23, 24). It is not clear what this phrase means, e.g., how is the distance of 90 to 400 bp measured in the phrase "as measured".

B) Claim 40 is indefinite over the recitation of "from 90 to 400 nucleotides as measured or 3' to 3'..." (line 15). It is not clear what this phrase means, e.g., how is the distance of 90 to 400 bp measured in the phrase "as measured".

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 28, 33, 36, 37, 38 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Frank et al. (Methods in Pathology, vol. 5, pp. 449-454, 1992; cited in the IDS and in the previous office action) as evidenced by Promega Catalog (page 67, 1993-93; cited in the previous office action).

Claims 33, 36, 37 and 40 are almost identical except for the differences in either the melting temperature of the primers or a length of the product, therefore claim 33 will be considered in detail, and specifics of claims 36, 37 and 40 will be pointed out separately.

Regarding claim 33, Frank et al. teach method for the simultaneous amplification and subsequent simultaneous detection of first target DNA and a second target DNA comprising (Frank

et al. teach simultaneous amplification and simultaneous detection of three different target nucleic acids using three different primer pairs. The target nucleic acids are: 1) cytomegalovirus (CMV) major immediate early (MIE) gene, 2) CMV late antigen gp64 (LA) gene and 3) human β-hemoglobin gene (page 449, third paragraph).):

A) simultaneously subjecting the denatured opposing strands of a first target DNA and the denatured opposing strands of a second target DNA to polymerase chain reaction in the presence of (Frank et al. teach simultaneously subjecting the denatured strands of all three templates to polymerase chain reaction (page 450, fifth paragraph):

i) an aqueous composition buffered to a pH of from 7 to 9 (Frank et al. teach a PCR reaction which contained 10% of 10x Taq DNA polymerase buffer (from Promega). Frank et al. do not specifically teach the pH of buffer being from 7 to 9, but as evidence by the Promega catalog, the reaction buffer has pH of (page 67), therefore Frank et al. teach this limitation).), and comprising, in the same solution:

first and second primers which are specific to and hybridizable with, respectively, first and second nucleic acid sequences which are in opposing strands of a first target DNA and which are separated from each other along said opposing strands by from 90 to 400 nucleotides as measured 5' to 5' (Frank et al. teach a pair of primers, CMV MIE (1st round), which are hybrizable to the opposing strands of the CMV LA gene, and are separated by 132 bp as measured 5' to 5' (Table 1).),

third and fourth primers which are specific to and hybridizable with, respectively, third and fourth nucleic acid sequences which are in opposing strands of a second target DNA which is the same as or different from said first target DNA, said third and fourth

nucleic acid sequences being different from said first and second nucleic acid sequences and being separated from each other along said opposing strands of said second target DNA by from 90 to 400 nucleotides as measured 5' to 5' (Frank et al. teach a pair of primers, hemoglobin (1st round), which are hybrizable to the opposing strands of the hemoglobin gene, and are separated by 210 bp as measured 5' to 5' (Table 1).),

wherein each of said first, second, third and fourth primers having a T_m within the range of from 65 to 74°C, as calculated by the formula T_m(°C) =67.5 + 0.34 (% G + C) - 395/N, all of said primer T_m's being within about 5°C of each other, said first and second primers having nucleotide lengths which differ from each other by no more than 5 nucleotides, and said third and fourth primers having nucleotide lengths which differ from each other by no more than 5 nucleotides (Frank et al. teach both sets of primers having nucleotide lengths within 5 bp from each other, as the CMV LA primers are 22 and 21 bp long, and the hemoglobin primers are 21 and 23 bp long (Table 1). Frank et al. do not specifically teach the melting temperatures of the primers, but they were calculated by the examiner using the formula required by the claim limitation, and were found to be within 3.3°C of each other, therefore anticipating the limitation of melting temperatures within about 5°C. See table below.), and

ii) the additional PCR reagents: a thermostable DNA polymerase, a DNA polymerase cofactor and dNTP's, any or all of said additional PCR reagents being supplied in the same or a different composition as defined in i), to simultaneously amplify said opposing first target DNA strands and said opposing second target DNA strands, provided that in each PCR cycle, each of priming and primer extension are carried out at a temperature within the range of from 62 to 75°C (Frank et al. teach a PCR reaction which

contained 200 μM of each dNTP, 5 units of Taq polymerse. Frank et al. do not explicitly teach Taq DNA polymerase cofactor, Mg^{2+} or Mn^{2+}. Frank et al. teach using 10x Taq polymerase buffer from Promega. As evidenced by 1992-93 Promega catalog, the 10x polymerase buffer contained $MgCl_2$ (page 67). The PCR reaction parameters for the first round included 2 minutes at 64°C for primer annealing and 2 minutes at 72°C for primer extension, anticipating the range from 62 to 75°C (page 450, paragraphs 3 and 4).),

B) simultaneously detecting at least one of said amplified first target DNA strands and at least one of said amplified second target DNA strands as a simultaneous determination of the presence of said first and second target DNA's (Frank et al. teach simultaneous detection of the amplification products by electrophoresis on a 3% NuSieve/1% agarose gel containing 0.5 μg/mL ethidium bromide (Fig. 1; page 451, first paragraph).).

Regarding claim 36, which differs from claim 33 by the limitation of primers having melting temperatures within about 2°C of each other, Frank et al. teach the CMV LA and hemoglobin primers with T_ms within 3.3°C of each other, therefore anticipating the limitation of melting temperatures within about 2°C (see Table below).

Regarding claim 37, which differs from claim 33 by the limitation of primers being separated from each other by 90 to 400 bp as measured 3' to 3', Frank et al. teach the CMV LA and hemoglobin primers separated by 132 and 165 bp, respectively, on the opposite strands of the target DNA (Table 1), and their melting temperatures are within 3.3°C of each other, therefore anticipating the limitation of melting temperatures within about 5°C (see Table below).

Regarding claim 40, which differs from claim 37 by the limitation of primers having melting temperatures within about 2°C of each other, Frank et al. teach the CMV LA and hemoglobin primers separated by 132 and 165 bp, respectively, on the opposite strands of the target DNA (Table

1), and their melting temperatures are within 3.3°C of each other, therefore anticipating the limitation of melting temperatures within about 2°C (see Table below).

Primer	Primer length, bp	T_m, °C	Product size (5' to 5'), bp
CMV MIE 5' (1st round)	20	73.25	162
CMV MIE 3' (1st round)	20	73.25	
CMV LA 5' (1st round)	22	69.6	132
CMV LA 3' (1st round)	21	71.4	
Hemoglobin 5'(1st round)	22	69.6	210
Hemoglobin 3'(1st round)	23	68.1	

Regarding claims 28 and 38, Frank et al. teach amplification of three DNA targets, CMV MIE gene, CMV LA gene and hemoglobin gene, with three primer sets for first round of amplification, where the primers have melting temperatures in the range of 65 to 74 °C and within 5.15°C of each other (anticipating the limitation of about 5°C), as well as lengths which differ from each other by no more than 5 nucleotides.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 29 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frank et al. and Picone et al. (WO 92/11273).

A) Teachings of Frank et al. are described above. Frank et al. teach detection of amplification products on Southern blots with probes complementary to the amplified fragments, but do not teach capture probes on solid support or probes having from 10 to 40 nucleotides and T_ms

greater than about 50°C, being hybridizable to a nucleic acid sequence at a temperature in the range of from 40 to 55°C.

B) Regarding claims 29 and 39, Picone et al. teach amplification products by hybridization, using multiple capture probes immobilized on solid support (page 6, lines 10-19; page 7, lines 11-19), which can detect different species within the same genus of pathogens or more than one genus. Picone et al. teach probes for the detection of amplified Legionella genes having lengths of 18 bp and melting temperatures of 58 and 60 °C (page 28, lines 20-24), the hybridization conditions being 20 minutes at 50-55°C (page 32, lines 30-36).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used the capture probes designed according to Picone et al. in the method of Frank et al. The motivation to do so, provided by Picone et al., would have been that multiple specific capture probes allowed specific detection of target nucleic acids under stringent conditions. As stated by Picone et al., "Without this invention, the different capture probes would normally be immobilized individually on a solid support. As a result, the assay would require the use of more test sample, more time to perform the test and more interpretation by the user." (page 6, lines 10-19).

11. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

The examiner will move to the new office in Alexandria on January 8, 2004. The new phone number in that office is (571) 272-0789. Gary Benzion will move to the new office on January 22, 2004. His new phone number is (571) 272-0782.

TS
December 20, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER

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